

AMENDMENTS TO THE SPECIFICATION

Please amend the first paragraph of the specification as follows:

This application is a 35 U.S.C. § 371 filing of PCT/US2005/003245, filed February 3, 2005. PCT/US2005/003245 claims the benefit of the following U.S. Applications: 60/542,780, filed February 5, 2004; 60/556,831 filed March 26, 2004; and 60/575,919 filed June 1, 2004. This application is also a continuation of U.S. Application No. and 10/912,932 filed August 6, 2004. The disclosures of all of the aforementioned applications are incorporated by reference in their entireties for all purposes.

Please amend the paragraph beginning on page 26, line 22 as follows:

Techniques for determining nucleic acid and amino acid sequence identity are known in the art. Typically, such techniques include determining the nucleotide sequence of the mRNA for a gene and/or determining the amino acid sequence encoded thereby, and comparing these sequences to a second nucleotide or amino acid sequence. Genomic sequences can also be determined and compared in this fashion. In general, identity refers to an exact nucleotide-to-nucleotide or amino acid-to-amino acid correspondence of two polynucleotides or polypeptide sequences, respectively. Two or more sequences (polynucleotide or amino acid) can be compared by determining their percent identity. The percent identity of two sequences, whether nucleic acid or amino acid sequences, is the number of exact matches between two aligned sequences divided by the length of the shorter sequences and multiplied by 100. An approximate alignment for nucleic acid sequences is provided by the local homology algorithm of Smith and Waterman, *Advances in Applied Mathematics* 2:482-489 (1981). This algorithm can be applied to amino acid sequences by using the scoring matrix developed by Dayhoff, *Atlas of Protein Sequences and Structure*, M.O. Dayhoff ed., 5 suppl. 3:353-358, National Biomedical Research Foundation, Washington, D.C., USA, and normalized by Gribskov, *Nucl. Acids Res.* 14(6):6745-6763 (1986). An exemplary implementation of this algorithm to determine percent identity of a sequence is provided by the Genetics Computer Group (Madison, WI) in the "BestFit" utility application. The default parameters for this method are described in the Wisconsin Sequence Analysis Package Program Manual, Version 8 (1995) (available from Genetics Computer Group,

Madison, WI). A preferred method of establishing percent identity in the context of the present disclosure is to use the MPSRCH package of programs copyrighted by the University of Edinburgh, developed by John F. Collins and Shane S. Sturrok, and distributed by IntelliGenetics, Inc. (Mountain View, CA). From this suite of packages the Smith-Waterman algorithm can be employed where default parameters are used for the scoring table (for example, gap open penalty of 12, gap extension penalty of one, and a gap of six). From the data generated the "Match" value reflects sequence identity. Other suitable programs for calculating the percent identity or similarity between sequences are generally known in the art, for example, another alignment program is BLAST, used with default parameters. For example, BLASTN and BLASTP can be used using the following default parameters: genetic code = standard; filter = none; strand = both; cutoff = 60; expect = 10; Matrix = BLOSUM62; Descriptions = 50 sequences; sort by = HIGH SCORE; Databases = non-redundant, GenBankGENBANK™ + EMBL + DDBJ + PDB + GenBankGENBANK™ CDS translations + Swiss protein + Spupdate + PIR. Details of these programs can be found on the at the following internet address: <http://www.ncbi.nlm.gov/cgi-bin/BLAST>. With respect to sequences described herein, the range of desired degrees of sequence identity is approximately 80% to 100% and any integer value therebetween. Typically the percent identities between sequences are at least 70-75%, preferably 80-82%, more preferably 85-90%, even more preferably 92%, still more preferably 95%, and most preferably 98% sequence identity.

Please amend the paragraph beginning on page 98, line 10 as follows:

For quantitative RT-PCR analysis, total RNA was isolated from dox-treated and untreated cells using the High Pure HIGHPURE™ Isolation Kit (Roche Molecular Biochemicals), and 25 ng of total RNA from each sample was subjected to real time quantitative RT-PCR to analyze endogenous gene expression, using TaqMan® assays. Probe and primer sequences are shown in Table 13. Reactions were carried out on an ABI 7700 SDS machine (PerkinElmer Life Sciences) under the following conditions. The reverse transcription reaction was performed at 48°C for 30 minutes with MultiScribe reverse transcriptase (PerkinElmer Life Sciences), followed by a 10-minute denaturation step at 95°C. Polymerase chain reaction (PCR) was carried out with AmpliGold DNA polymerase (PerkinElmer Life Sciences) for 40 cycles at

95°C for 15 seconds and 60°C for 1 minute. Results were analyzed using the SDS version 1.7 software and are shown in Figure 27, with expression of the eGFPmut gene normalized to the expression of the human GAPDH gene. A number of cell lines exhibited doxycycline-dependent expression of eGFP; line 18 (T18) was chosen as a model cell line for further studies.

Please amend the paragraph beginning on page 99, line 20 as follows:

The T18 stable cell line (Example 9) was transfected with one or both of the ZFP-FokI expression plasmid (pcDNA3.1-GFP287-FokI and pcDNA3.1-GFP296-FokI, Example 7) and 300 ng of the donor plasmid pCR(R)4-TOPO-GFPdonor5 (Example 10) using LipofectAMINE LIPOFECTAMINE™ 2000 Reagent (Invitrogen) in Opti-MEM OPTI-MEM™ I reduced serum medium, according to the manufacturer's protocol. Expression of the defective chromosomal eGFP gene was induced 5-6 hours after transfection by the addition of 2 ng/ml doxycycline to the culture medium. The cells were arrested in the G2 phase of the cell cycle by the addition, at 24 hours post-transfection, of 100 ng/ml Nocodazole (Figure 30) or 0.2 uM Vinblastine (Figure 31). G2 arrest was allowed to continue for 24-48 hours, and was then released by the removal of the medium. The cells were washed with PBS and the medium was replaced with DMEM containing tetracycline-free FBS and 2 ng/ml doxycycline. The cells were allowed to recover for 24-48 hours, and gene correction efficiency was measured by monitoring the number of cells exhibiting eGFP fluorescence, by fluorescence-activated cell sorting (FACS) analysis. FACS analysis was carried out using a Beckman-Coulter EPICS™ XL-MCL instrument and System II Data Acquisition and Display software, version 2.0. eGFP fluorescence was detected by excitation at 488 nm with an argon laser and monitoring emissions at 525 nm (x-axis). Background or autofluorescence was measured by monitoring emissions at 570 nm (y-axis). Cells exhibiting high fluorescent emission at 525 nm and low emission at 570 nm (region E) were scored positive for gene correction.

Please amend the paragraph beginning at page 113, line 22 as follows:

Briefly, a cDNA pool generated from 293 and U2OS cells was used in five separate amplification reactions, each using a different set of amplification primers specific to the Ku70 gene, to generate five pools of cDNA fragments (pools A-E), ranging in size from 500-750 bp.